Diabetes Mellitus in CKD: Kidney Early Evaluation Program (KEEP) and National Health and Nutrition and Examination Survey (NHANES) 1999-2004

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Background: Diabetes mellitus is the leading cause of chronic kidney disease (CKD) and contributes to increased morbidity and mortality in the CKD population. Early diabetes identification through targeted screening programs is important for the development of preventive strategies.

Methods: This is a cross-sectional analysis of the National Kidney Foundation Kidney Early Evaluation Program (KEEP) data and National Health and Nutrition and Examination Survey (NHANES) 1999-2004 data. KEEP is a community-based health-screening program enrolling individuals 18 years or older with diabetes, hypertension, or family history of kidney disease, diabetes, or hypertension. Study participants were those identified as meeting these inclusion criteria. Participants who had received kidney transplants or were currently receiving dialysis therapy were excluded.

Results: Of 73,460 KEEP participants, 20,562 (28.0%) had diabetes compared with 1,545 of 17,049 (6.7%) NHANES participants. Age, obesity, high cholesterol level, hypertension, and cardiovascular disease distributions were similar for patients with diabetes in both populations, whereas women and African Americans were overrepresented in KEEP. The prevalence of diabetes in KEEP progressively increased with increasing stage of CKD, and this relationship persisted in subgroup analyses of older participants (age $>$ 46 years), as well as in analyses stratified by sex, race, and other CKD risk factors: current tobacco use, obesity, hypertension, cardiovascular disease, and increased cholesterol level. KEEP participants with CKD who reported having diabetes were unlikely to have met target blood glucose levels (odds ratio, 0.71; 95% confidence interval, 0.66 to 0.77; $P < 0.001$). Reporting not having diabetes was associated with the likelihood of increased blood glucose levels (odds ratio, 1.28; 95% confidence interval, 1.16 to 1.41; $P < 0.001$).

Conclusion: KEEP is congruent with NHANES regarding a greater prevalence of diabetes in patients with CKD. As a targeted screening program, KEEP may represent a higher risk and more motivated patient population.

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INDEX WORDS: Chronic kidney disease; diabetes mellitus; Kidney Early Evaluation Program (KEEP); National Health and Nutrition Examination Survey (NHANES); screening.

Approximately 21 million persons in the United States are known to have diabetes mellitus, which contributes to an increasing health care burden. Diabetes mellitus, both type 1 and type 2, is the leading cause of chronic kidney disease (CKD). The hallmark of diabetic kidney disease onset, the presence of microalbuminuria (albumin, 30 to 299 mg/g by spot urine albumin-creatinine ratio), is found in approximately 45% of patients with diabetes.[1] The presence of overt macroalbuminuria (albumin $>$ 300 mg/g) is found in approximately 8%. However, diabetes ac-

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counts for about 30% to 40% of CKD and up to 45% of end-stage renal disease cases.[1,2]

Recognition of CKD as an increasing public health problem highlights the need for early awareness and detection. Approximately 400,000 persons in the United States received renal replacement therapy (dialysis or transplantation) for treatment of end-stage renal disease in 2000,[3] and by 2030, this number may increase to more than 2 million, with a marked impact on health care expenditures.[4] The estimated prevalence of earlier CKD stages (stages 1 to 4) in US adults was 24 to 28 million, with many millions more at risk based on the National Health and Nutrition Examination Survey (NHANES) 1999-2004.[4]

Diabetic kidney disease often accompanies other comorbid conditions, particularly the other traditional Framingham cardiovascular disease (CVD) risk factors: hypertension, dyslipidemia, tobacco use, and increasing age. In addition, the presence of diabetes mellitus associated with CKD can be associated with nontraditional risk factors, such as mineral metabolism disorders, anemia, secondary hyperparathyroidism, and uremia.[4-6] Collectively, these comorbid conditions contribute to the overall high morbidity and mortality associated with diabetes-related CKD.[6,7]

CKD often is silent and undetected until advanced stages, and many patients with CKD are identified only shortly before the onset of symptomatic uremia, when opportunities to prevent adverse outcomes are few.[8] Detection of CKD at earlier stages would allow more time for evaluation and treatment. To identify individuals at greatest risk of CKD, the Kidney Early Evaluation Program (KEEP) was developed by the National Kidney Foundation to provide screening for early CKD.[9,10] KEEP is a free, voluntary, community-based kidney health screening program designed to raise awareness and detection of kidney disease in high-risk individuals, those with diabetes mellitus or hypertension or a first-order relative with diabetes, hypertension, or kidney disease. Participants are recruited based on their perceived risk.

In this report of the KEEP database, we sought to define baseline characteristics of diabetes mellitus in the CKD population and associated comorbid conditions in comparison to NHANES 1999-2004, a representative sample of patients with CKD in the United States for which participants are randomly selected and then volunteer to participate.

METHODS

KEEP and NHANES Study Participants

We included only eligible KEEP participants from August 2000 through December 31, 2006, from 47 National Kidney Foundation affiliates and 1,608 screening programs in 49 states and the District of Columbia. The KEEP study cohort in this study, excluding individuals with missing data values, includes 73,460 eligible KEEP participants. For comparison purposes with KEEP data, all samples analyzed using data collected in NHANES 1999-2004 were restricted to individuals aged 18 years or older (n = 17,061). For all analyses using smoking status, self-reported kidney disease, or self-reported CVD, the NHANES study population was limited to participants aged 20 years or older (n = 15,332). The KEEP program and the NHANES database are fully described elsewhere in this supplement.[11]

Definitions

To ensure consistent and unbiased comparisons between KEEP and NHANES participants, we applied common definitions for comorbid conditions used in the analyses, with some minor exceptions. Estimated glomerular filtration rate (eGFR) was calculated using the modified Modification of Diet in Renal Disease Study equation,[12] and serum creatinine was calibrated to the Cleveland Clinic Research Laboratory.[13] Albumin-creatinine ratios were calculated from urine samples and recorded as less than 30, 30 to 300, or greater than 300 mg/g. CKD stages were defined as follows: stage 1, eGFR of 90 mL/min/1.73 m^2 or greater ($\geq$1.50 mL/s/1.73 m^2) and albumin-creatinine ratio of 30 mg/g or greater; stage 2, eGFR of 60 to 89 mL/min/1.73 m^2 (1.00 to 1.48 mL/s/1.73 m^2) and albumin-creatinine ratio of 30 mg/g or greater; stage 3, eGFR of 30 to 59 mL/min/1.73 m^2 (0.50 to 0.98 mL/s/1.73 m^2); stage 4, eGFR of 15 to 29 mL/min/1.73 m^2 (0.25 to 0.48 mL/s/1.73 m^2); and stage 5, eGFR less than 15 mL/min/1.73 m^2 ($<$0.25 mL/s/1.73 m^2). Diabetes was defined as history of diabetes (self-report or retinopathy), use of medications to treat diabetes, or newly diagnosed diabetes defined as fasting blood glucose level of 126 mg/dL or greater ($\geq$7.0 mmol/L) or nonfasting blood glucose level of 200 mg/dL or greater ($\geq$11.1 mmol/L) in the absence of self-report of medicine use. Increased blood glucose was defined as fasting blood glucose level of 127 mg/dL or greater ($\geq$7.0 mmol/L) or nonfasting blood glucose level of 140 mg/dL or greater ($\geq$7.8 mmol/L). Hypertension was defined as history of hypertension (self-report), use of medications to treat hypertension, or newly diagnosed hypertension (Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure),[14] defined as systolic blood pressure of 130 mm Hg or greater or diastolic blood pressure of 80 mm Hg or greater for persons with a history of diabetes or CKD, otherwise systolic blood pressure of 140 mm Hg or greater or diastolic blood pressure of 90 mm Hg or greater. History of CVD was defined as self-reported history of heart attack,

Table 1. Demographic Characteristic Distribution by Diabetes Mellitus Status

Characteristics	Cohort			
	KEEP		NHANES 1999-2004	
	Diabetes (n = 20,562)	No Diabetes (n = 52,874)	Diabetes (n = 1,545)	No Diabetes (n = 15,504)
Age (y)				
18-30	2.6	10.2	2.7	25.5
31-45	13.7	25.8	15.0	31.8
46-60	36.5	34.6	34.0	24.4
61-75	36.4	21.9	34.0	12.4
>75	10.8	7.5	14.3	6.0
Sex				
Men	33.3	30.9	48.3	48.0
Women	66.7	69.1	51.7	52.0
Race/ethnicity				
White	47.2	46.4	64.8	71.9
African American	32.3	34.9	16.2	10.8
Others	20.5	18.8	19.0	17.3
Hispanic	12.3	12.3	13.8	13.2
Non-Hispanic	87.7	87.7	86.2	86.8
Education				
<High school	20.5	13.6	34.6	20.6
≥High school	79.5	86.4	65.4	79.4
Risk factors				
Current smoker	10.8	12.7	19.9	25.2
Obesity*	56.4	39.5	54.3	29.1
Hypertension	68.7	47.6	62.5	23.7
Cardiovascular disease	29.9	15.9	29.0	7.4
Increased cholesterol	61.0	41.1	59.2	35.7
All	100	100	100	100

Note: Categorical values are expressed in percent. In KEEP, the presence of diabetes is defined as self-reported history of diabetes mellitus, receiving medication for diabetes mellitus, or fasting blood glucose level of 126 mg/dL or greater or nonfasting blood glucose level of 200 mg/dL or greater. In NHANES 1999-2004, diabetes is defined as self-reported diabetes. To convert blood glucose from mg/dL to mmol/L, multiply by 0.0555.

Abbreviations: KEEP, Kidney Early Evaluation Program; NHANES, National Health and Nutrition and Examination Survey.

*Body mass index of 30 kg/m^2 or greater.

heart angioplasty, bypass surgery, heart failure, abnormal heart rhythm, or stroke. (NHANES defined history of CVD as self-reported history of coronary heart disease, angina/angina pectoris, heart attack, congestive heart failure, or stroke.) Obesity was defined as body mass index of 30 kg/m^2 or greater.

Statistical Analysis

We examined the prevalence of diabetes in KEEP and NHANES participants. Descriptive statistics are reported as counts and proportions in both the KEEP and NHANES data sets. The prevalence of diabetes was determined overall and separately for patients with CKD stages 1/2, 3, 4, and 5. Logistic regression was used to analyze the association of risk factors with increased blood glucose levels in self-reported nondiabetic KEEP participants and the association of risk factors for self-reported diabetes in KEEP participants meeting a targeted blood glucose level. The controlled risk factors in logistic regressions were age, sex, race, smoking history, self-reported hypertension, family history of diabetes and hypertension, obesity, CKD status, cohort years, and region. *P* less than 0.05 is considered statistically significant. To obtain national estimates of each statistic in NHANES, sampling weights and survey design were implemented by SUDAAN (Research Triangle Institute, Research Triangle Park, NC).

RESULTS

Of 73,460 KEEP participants, 20,562 (28.0%) were found to have diabetes mellitus, as were 1,545 of the 17,049 (6.7%) NHANES participants (Table 1). In participants in both KEEP and NHANES with diabetes, the age distribution was similar, whereas women and African Americans were overrepresented in KEEP. KEEP participants had greater educational achievement and

Table 2. Prevalence of Diabetes Mellitus

	Diabetes Mellitus			
	KEEP		NHANES 1999-2004	
Characteristics	No. of Participants	%	No. of Participants	%
Age (y)				
18-30	526	8.9	37	0.8
31-45	2,816	17.1	158	3.3
46-60	7,508	29.1	354	9.1
61-75	7,494	39.3	682	16.5
>75	2,218	36.0	314	14.6
Sex				
Men	6,833	29.5	754	6.7
Women	13,712	27.3	791	6.7
Race/ethnicity				
White	9,492	28.4	624	6.1
African American	6,483	26.4	378	9.7
Others	4,114	29.8	543	7.3
Hispanic	2,536	28.0	498	7.0
Non-Hispanic	18,026	28.0	1,047	6.7
Education				
<High school	4,141	36.9	759	10.8
≥High school	16,090	26.3	782	5.6
Risk factors				
Current smoker	2,093	24.9	254	5.6
Obesity*	11,410	35.8	658	11.7
Hypertension	13,940	36.1	990	16.0
Cardiovascular disease	6,147	42.2	485	22.6
Increased cholesterol	1,458	41.3	735	14.3
All	20,562	28.0	1,545	6.7

Note: In KEEP, the presence of diabetes is defined as self-reported history of diabetes mellitus, receiving medication for diabetes mellitus, or fasting blood glucose level of 126 mg/dL or greater or nonfasting blood glucose level of 200 mg/dL or greater. In NHANES 1999-2004, diabetes is defined as self-reported diabetes. To convert blood glucose from mg/dL to mmol/L, multiply by 0.0555.

Abbreviations: KEEP, Kidney Early Evaluation Program; NHANES, National Health and Nutrition and Examination Survey.

*Body mass index of 30 kg/m^2 or greater.

less tobacco use, whereas obesity, hypertension, CVD, and increased cholesterol levels were similar between KEEP and NHANES.

Overall, the demographic percent prevalence of diabetes mellitus in patients with CKD for age, sex, race, and level of education was similar between KEEP and NHANES (Table 2). However, in assessing comorbid risk factors, percent prevalence of participants who were current smokers, obese, or had hypertension, CVD, or increased cholesterol level was greater in KEEP than NHANES. Of note, there was a graded relationship with increasing prevalence of diabetes mellitus with increasing age (except age > 75 years) in both KEEP and NHANES.

On assessment of demographic and self-reported risk factors by CKD stage, we found a greater percentage of responders in stage 3 than the other stages (Table 3). There is an inverse relationship between CKD stage and increasing age (Fig 1A). Prevalence by CKD stage decreased in the group aged 18 to 30 years (stage 1, 14.7; stage 2, 4.0; and stages 3 to 5, 3.1). Corresponding values for the other age groups are 31 to 45 years: stage 1, 8.4; stage 2, 6.1; stages 3 to 5, 6.6; 46 to 60 years: stage 1, 5.9; stage 2, 7.2; stages 3 to 5, 15.7; 61 to 75 years: stage 1, 2.3; stage 2, 8.3; stages 3 to 5, 33.6; and older than 75 years: stage 1, 1.3; stage 2, 8.7; and stages 3 to 5, 50.1. There also is a consistent graded relationship between reported tobacco use, obesity, hypertension, CVD, and advancing CKD stage (Fig 1B).

The presence of CKD in KEEP participants who reported not having diabetes was associated

Table 3. Prevalence of Diabetes Mellitus by Chronic Kidney Disease Stage

	Chronic Kidney Disease Stage*							
	KEEP†				NHANES 1999-2004‡			
Characteristics	None	Stage 1	Stage 2	Stages 3-5	None	Stage 1	Stage 2	Stages 3-5
Age (y)								
18-30	78.1	14.7	4.0	3.1	74.2	NR	NR	NR
31-45	78.9	8.4	6.1	6.6	69.2	16.9	NR	NR
46-60	71.3	5.9	7.2	15.7	64.8	10.9	13.3	11.0
61-75	55.8	2.3	8.3	33.6	49.1	6.5	14.0	30.5
>75	39.9	1.3	8.7	50.1	28.6	NR	13.0	56.3
Sex								
Men	63.3	4.8	8.7	23.2	55.4	10.9	15.8	17.8
Women	63.0	4.5	7.0	25.5	56.0	7.8	9.8	26.4
Race/ethnicity								
White	61.1	2.8	6.9	29.2	56.0	6.9	12.2	24.9
African American	65.6	6.2	7.9	20.3	51.9	13.4	13.9	20.7
Others	64.1	6.3	8.7	21.0	57.5	14.9	13.8	13.8
Hispanic	68.2	6.9	8.3	16.6	56.4	16.4	15.8	11.4
Non-Hispanic	62.5	4.3	7.5	25.7	55.6	8.2	12.3	23.9
Education								
<High school	56.7	5.0	9.4	28.9	45.9	12.9	13.8	27.4
≥High school	64.8	4.5	7.0	23.7	60.5	7.7	12.3	19.6
Risk factors								
Current smoker	67.3	7.6	8.4	16.7	63.2	13.3	12.9	10.6
Obesity§	63.0	5.1	7.6	24.3	56.1	9.9	14.0	19.9
Hypertension	57.6	4.4	8.2	29.8	48.6	9.9	13.8	27.7
Cardiovascular disease	53.3	4.2	8.8	33.7	37.8	5.8	14.2	42.3
Increased cholesterol	63.4	3.7	7.5	25.4	55.5	8.9	12.1	23.5

Abbreviations: KEEP, Kidney Early Evaluation Program; NHANES, National Health and Nutrition and Examination Survey; NR, estimate not reliable.

*Chronic kidney disease stage determined by estimated glomerular filtration rate as described in Methods.

†Number of patients with diabetes and nonmissing estimated glomerular filtration rate value = 17,612.

‡Number of patients 18 years or older with self-reported diabetes and nonmissing glomerular filtration rate value = 1,302; number 20 years or older with self-reported diabetes and nonmissing glomerular filtration rate value = 1,294.

§Body mass index of 30 kg/m^2 or greater.

with the likelihood of having increased blood glucose levels (odds ratio [OR], 1.28; 95% confidence interval [CI], 1.16 to 1.41; $P < 0.001$; Table 4). On assessment by CKD stage, stages 1 and 2 were associated with the likelihood of nondiabetic participants having increased blood glucose levels (stage 1, OR, 1.94; 95% CI, 1.55 to 2.44; $P < 0.001$; stage 2, OR, 1.54; 95% CI, 1.28 to 1.84; $P < 0.001$; Fig 2). Similarly, stages 4 and 5 were associated with the likelihood of nondiabetic participants having increased blood glucose levels, but with larger CIs (stage 4, OR, 1.57; 95% CI, 1.01 to 2.43; $P = 0.04$; stage 5, OR, 2.5; 95% CI, 1.10 to 5.68; $P < 0.03$). Stage 3 nondiabetic participants were not associated with the likelihood of having increased blood glucose levels (OR, 1.09; 95% CI, 0.97 to 1.22; $P = 0.2$). Of note, nondiabetic participants older than 60 years, men, African Americans, and those reporting current tobacco use, family history of diabetes mellitus, hypertension, or obesity were all likely to have increased blood glucose levels (Table 4).

Overall, KEEP participants with CKD who reported having diabetes were unlikely to have met target blood glucose levels (OR, 0.71; 95%, CI 0.66 to 0.77; $P < 0.001$; Table 5). On assessment by CKD stage, patients with stages 1 to 4 were all unlikely to have met target blood glucose levels (stage 1, OR, 0.46; 95% CI, 0.39 to 0.55; $P < 0.001$; stage 2, OR, 0.56; 95% CI, 0.48 to 0.64; $P < 0.001$; stage 3, OR, 0.89; 95% CI, 0.81 to 0.97; $P < 0.01$; stage 4, OR, 0.58; 95% CI, 0.44 to 0.76; $P < 0.001$; and stage 5, OR,

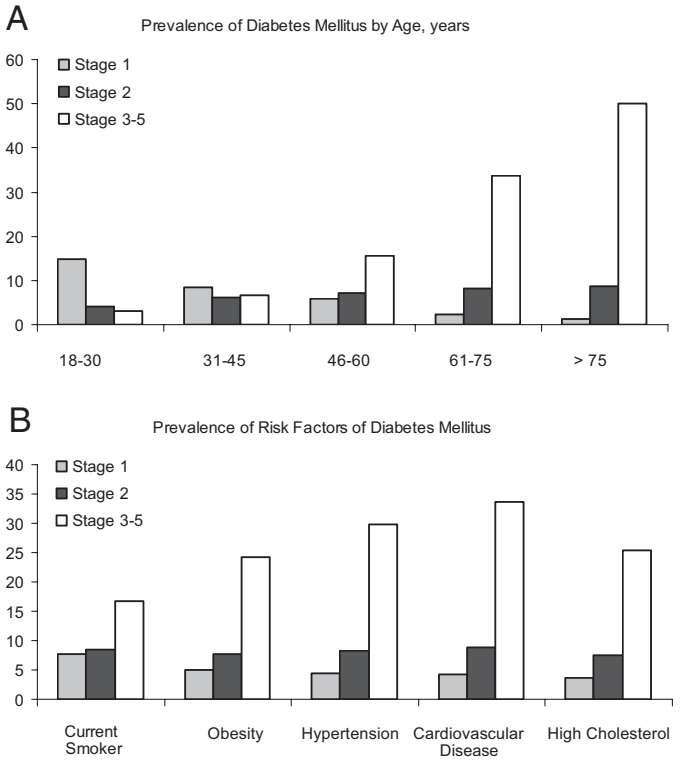

Figure 1. Prevalence of (A) self-reported diabetes mellitus by age and (B) self-reported risk factors observed in patients with diabetes mellitus. Data grouped by chronic kidney disease stages determined as follows: stage 1, estimated glomerular filtration rate (eGFR) of 90 mL/min/1.73 m^2 or greater and albumin-creatinine ratio (ACR) of 30 mg/g or greater; stage 2, eGFR of 60 to 89 mL/min/1.73 m^2 and ACR of 30 mg/g or greater; stage 3, eGFR of 30 to 59 mL/min/1.73 m^2; stage 4, eGFR of 15 to 29 mL/min/1.73 m^2; and stage 5, eGFR less than 15 mL/min/1.73 m^2. To convert eGFR from mL/min/1.73 m^2 to mL/s/1.73 m^2, multiply by 0.01667.

0.69; 95% CI, 0.36 to 1.34; $P = 0.3$; Fig 3). Of note, men and participants who reported having a family history of diabetes mellitus, hypertension, or obesity were all less likely to have met target blood glucose levels (Table 5).

DISCUSSION

The prevalence of self-reported diabetes mellitus was significantly greater in the KEEP population than the NHANES population. The 2 populations otherwise were comparable by age and sex, with subtle discrepancies in race, level of education, and male to female respondents. These data suggest that the KEEP health screening population is more enriched than NHANES with comorbid diabetes mellitus and CKD, largely because of the targeted nature of the screening program. Importantly, regarding the prevalence of comorbid risk factors in the diabetic population, there was a graded relationship between tobacco use, obesity, hypertension, CVD, and increased cholesterol levels and advancing CKD stage. In addition, there was an inverse relationship between increasing age and CKD stage. The prevalence of stage 1 CKD was greater in younger age groups and decreased with advancing age. The prevalence of stages 3 to 5 CKD was greater in older age groups. Overall, these data are consistent with our published reports and prior KEEP data reports.[15-20]

Although diabetes prevalence is greatest in persons 65 years and older, those younger than 45 years experienced the greatest increase in the last decade.[21] African American and Hispanic populations have a disproportionately greater prevalence and rate of increase in diabetes.[22] Although the United States has the greatest proportion of patients with diabetes, the rapid increase in diabetes prevalence is occurring globally, and soon more than 300 million persons worldwide will be affected.[21]

The finding that the presence of CKD in participants without diabetes was likely to be associated with increased blood glucose levels is particularly novel. This finding was stronger in patients with stages 1 and 2. However, stage 3, with the greatest prevalence and the most participants with CKD detected, was not associated with the likelihood of increased blood glucose levels in nondiabetic screening participants. The larger CIs in stages 4

Table 4. Odds of Nondiabetic Kidney Early Evaluation Program Participants Having Increased Blood Glucose

Characteristics	Odds Ratio (95% confidence interval)	*P*
Age (y)		
18-30	0.40 (0.32-0.50)	<0.001
31-45	0.65 (0.57-0.73)	<0.001
46-60	1	
61-75	1.33 (1.20-1.48)	<0.001
>75	1.51 (1.29-1.77)	<0.001
Sex		
Women	1	
Men	1.22 (1.11-1.33)	<0.001
Race		
White	1	
African American	1.28 (1.16-1.41)	<0.001
Other	1.56 (1.39-1.76)	<0.001
Risk factors		
Chronic kidney disease	1.28 (1.16-1.41)	<0.001
Current smoking	1.26 (1.11-1.43)	<0.001
Hypertension	1.22 (1.11-1.34)	<0.001
Family history of diabetes	1.25 (1.14-1.37)	<0.001
Family history of hypertension	0.87 (0.78-0.96)	0.008
Obesity*	1.59 (1.46-1.74)	<0.001

Note: Increased blood glucose defined as fasting blood glucose level of 127 mg/dL or greater or nonfasting blood glucose level of 140 mg/dL or greater. To convert blood glucose from mg/dL to mmol/L, multiply by 0.0555.

*Body mass index of 30 kg/m^2 or greater.

Table 5. Relative Risk of Diabetic Kidney Early Evaluation Program Participants Meeting Target Blood Glucose

	Relative Risk (95% confidence interval)	*P*
Age (y)		
18-30	1.52 (1.20-1.92)	<0.001
31-45	1.22 (1.09-1.36)	<0.001
46-60	1	
61-75	1.01 (0.93-1.09)	0.9
>75	1.08 (0.95-1.22)	0.2
Sex		
Women	1	
Men	0.74 (0.68-0.79)	<0.001
Race		
White	1	
African American	0.94 (0.87-1.02)	0.1
Other	0.76 (0.70-0.84)	<0.001
Risk factors		
Chronic kidney disease	0.71 (0.66-0.77)	<0.001
Current smoking	0.98 (0.87-1.09)	0.7
Hypertension	0.92 (0.85-1.00)	0.06
Family history of diabetes	0.79 (0.73-0.86)	<0.001
Family history of hypertension	1.22 (1.12-1.33)	<0.001
Obesity*	0.80 (0.74-0.86)	<0.001

Note: Target blood glucose was defined as fasting blood glucose level less than 127 mg/dL or nonfasting blood glucose level less than 140 mg/dL. To convert blood glucose from mg/dL to mmol/L, multiply by 0.0555.

*Body mass index of 30 kg/m^2 or greater.

and 5 likely are caused by low prevalence of detected CKD at these stages in the screening program as a whole. Current tobacco use, obesity, hypertension, CVD, or increased cholesterol levels were all associated with increased blood glucose levels in participants previously considered not to

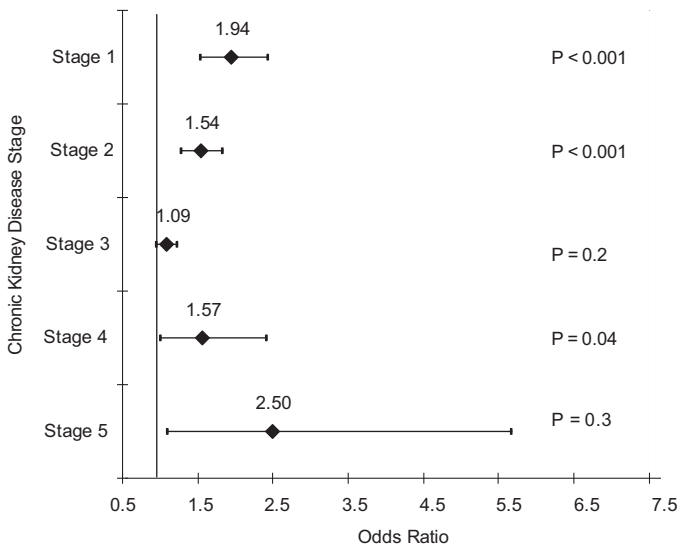

Figure 2. Adjusted odds ratios by chronic kidney disease stage for self-reported nondiabetic Kidney Early Evaluation Program (KEEP) participants of having increased fasting blood glucose levels of 127 mg/dL or greater or nonfasting levels of 140 mg/dL or greater. Chronic kidney disease stages determined as described in Fig 1. To convert blood glucose from mg/dL to mmol/L, multiply by 0.0555.

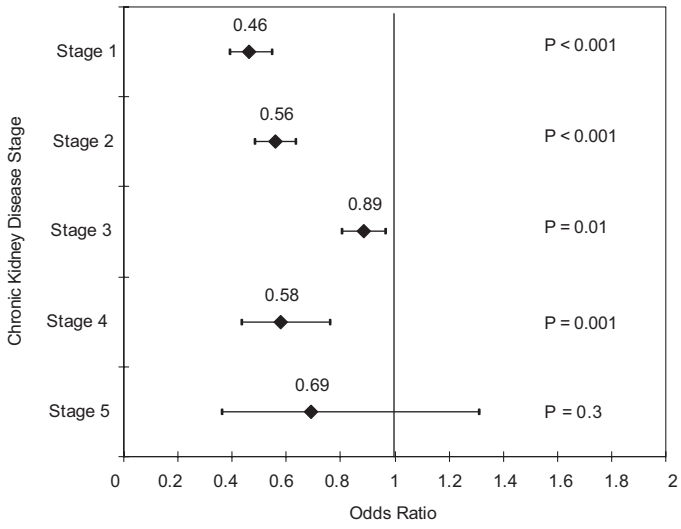

Figure 3. Adjusted odds ratios by chronic kidney disease stage for self-reported diabetic KEEP participants with target fasting blood glucose levels less than 127 mg/dL or nonfasting blood glucose levels less than 140 mg/dL. Chronic kidney disease stages determined as described in Fig 1. To convert blood glucose from mg/dL to mmol/L, multiply by 0.0555.

have diabetes. Interpretation of these data is limited because stages 1 to 3 are not stratified by level of albuminuria and stages 1 and 2 have smaller samples than stage 3, for which the association was not observed.

The observation from the KEEP database of increased undiagnosed diabetes in patients with CKD stages 1 and 2 is commensurate with prior work showing that microalbuminuria and lower levels of albuminuria are associated with obesity, insulin resistance, increased blood pressure, and dyslipidemia, all components of cardiometabolic syndrome. Microalbuminuria and early CKD, like other components of cardiometabolic syndrome, often include underlying states of oxidative stress and inflammation and endothelial dysfunction.

Microalbuminuria, present in 20% to 30% of patients with diabetes,[23] was recognized in recent years as a marker of endothelial injury and a harbinger for progression to CKD. Microalbuminuria occurs contemporaneously with increased capillary permeability secondary to endothelial damage.[24] The appearance of microalbuminuria clusters with other markers of endothelial dysfunction and other components of cardiometabolic syndrome.[25,26] A recent study of patients with type 2 diabetes mellitus showed that urinary albumin excretion in men was associated strongly with insulin resistance.[27]

Participants who reported having diabetes in this CKD screening population also were likely not to have met target blood glucose levels at all stages except stage 5. Again, the large CI likely is caused by a lower prevalence of detection observed at this stage. Interestingly, participants who reported a family history of diabetes, hypertension, or obesity were likely not to have met target blood glucose levels, but not those who reported current tobacco use or hypertension.

Collectively, these data suggest that prior population analysis underestimated the extent of diabetes coexisting with CKD. This is particularly true if we include persons with increased fasting glucose levels who had not had a diagnosis of diabetes. KEEP has the limitations common to population-screening studies. Screened participants are volunteers who likely were motivated by their recognized risk of CKD. Thus, diabetes rates were greater, and this may have influenced other results. However, we believe that the targeted nature of the KEEP screening program and the large sample size with clinical characteristics similar to the NHANES database accurately defines the diabetic CKD population in the United States. In addition, this report may herald how NHANES reports in the future with respect to diabetes prevalence and its relationship to CKD.

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